MTN-003

Adverse Event Reporting and Source Documentation

VOICE Operational Walkthrough
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Protocol Section 8.2

- Study site staff will document in source documents all adverse events (AEs) reported by or observed in enrolled study participants regardless of severity and presumed relationship to study product

- Study staff also will report on case report forms the following subset of AEs reported by or observed in enrolled participants

Protocol Section 8.2

- All genital, genitourinary, and reproductive system AEs
- All fractures
- All AEs of severity grade 2 or higher in the following categories: dizziness, headache, nausea, vomiting, diarrhea, abdominal pain, rash
- All AEs of severity grade 3 or higher

Protocol Section 8.2

- All serious AEs, as defined by ICH GCP

ICH Definition of Serious

- Any untoward medical occurrence that at any dose:
  - Results in death
  - Is life-threatening
  - Requires inpatient hospitalization or prolongs an existing hospitalization
  - Results in persistent or significant disability/incapacity
  - Is a congenital anomaly/birth defect
- Important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the outcomes listed in the definition above also should usually be considered serious

Protocol Section 8.2

- All serious AEs, as defined by ICH GCP

- All AEs that result in permanent discontinuation of study product use

- All lab test abnormalities not otherwise associated with a reported clinical AE

- AEs that do not meet the above-listed criteria but do meet expedited reporting requirements per protocol Section 8.3

Protocol Section 8.3

- This study uses the standard level of expedited AE reporting as defined in the DAIDS EAE Manual
  - Same as Phase IIb portion of HPTN 035
  - Same as MTN-001

Protocol Section 8.2

- AE severity will be graded per the DAIDS Table for Grading Adult and Pediatric Adverse Events and the Female Genital Grading Table for Use in Microbicide Studies except that asymptomatic BV will not be a reportable AE

Look in the FGGT first, then use the standard DAIDS Toxicity Table if the AE does not appear in the FGGT

Fun Time

AE Reporting in MTN-003

Reportable?

- Grade 1 AST   ☒Yes   ☐No
- Grade 1 headache   ☐Yes   ☒No
- Grade 2 headache   ☒Yes   ☐No
- Grade 1 nausea   ☐Yes   ☒No
- Grade 2 nausea   ☒Yes   ☐No
- Grade 1 abdominal pain ☐Yes   ☒No
- Grade 2 abdominal pain ☒Yes   ☐No
- Grade 1 bacterial vaginosis ☐Yes ☒No
- Grade 2 bacterial vaginosis ☒Yes ☐No

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AE Reporting in MTN-003

Reportable?

- Grade 2 cough   ☐ Yes   ☒ No
- Grade 2 fracture of forearm   ☒ Yes   ☐ No
- Grade 2 mastitis   ☒ Yes   ☐ No
- Grade 2 musculoskeletal pain   ☐ Yes   ☒ No
- Grade 2 decreased hemoglobin   ☒ Yes   ☐ No
- Grade 2 urinary tract infection   ☒ Yes   ☐ No
- Grade 2 skin ulcer (on ankle)   ☐ Yes   ☒ No
- Grade 2 vulvar ulcer   ☒ Yes   ☐ No

AE Reporting in MTN-003

Reportable?

- Grade 2 pneumonia treated in OPD ☐Yes ☒No
- Grade 2 pneumonia treated in hospital ☒Yes ☐No
- Grade 2 upper respiratory infection ☐Yes ☒No
- Grade 2 vaginal trichomoniasis ☒Yes ☐No
- Grade 2 hepatitis B infection ☒Yes ☐No
- Grade 2 malaria ☐Yes ☒No
- Grade 3 malaria ☒Yes ☐No
- Grade 3 upper respiratory infection ☒Yes ☐No
- Grade 4 asthma attack (bronchospasm) ☒Yes ☐No

Limited AE Reporting

- Site SOPs for safety monitoring and AE reporting should reflect limited AE reporting
- Site SOPs for source documentation should also reflect limited AE reporting

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AE Documentation

- Regardless of reporting on CRFs, identify, document, and follow all AEs to resolution or stabilization

    - <u>For each AE</u>, source documentation should include AE term/diagnosis, severity grade, onset date, outcome, outcome date, treatment

    - <u>For AEs reported on CRFs</u>, source documentation also must include date reported to site, relationship to study product, action taken with study product, whether the AE is an SAE, whether the AE is an EAE (all of these data are recorded on the AE Log form)

Limited AE Reporting

- Site SOPs for source documentation should reflect limited AE reporting:
  - Because some AEs will not be reported on case report forms, the AE Log form cannot be designated as source for all data elements
  - Identify in SOPs what document will serve as source for each data element

AE Documentation

- Use AE tracking tools to ensure all AEs are properly documented and all reportable AEs are reported on the AE Log case report form

What are your questions?